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Dkt. 0575/65219-A/JPW/PJP/PL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Michael R. Rosen, et al

U.S. Serial No.: 09/898,417

Examiner: B. Whiteman

Filed: July 3, 2001

Group Art Unit: 1635

For: A HIGH THROUGHPUT BIOLOGICAL HEART RATE  
MONITOR THAT IS MOLECULARLY DETERMINED

1185 Ave of the Americas  
New York, New York 10036  
June 4, 2003.

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

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SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

This Second Supplemental Information Disclosure Statement is submitted under 37 C.F.R. §1.97(c) and 37 C.F.R. §1.97(e)(2) to supplement the Information Disclosure Statements filed on May 2, 2003 and October 3, 2002.

According to 37 C.F.R. §1.97(c), an Information Disclosure Statement shall be considered by the U.S. Patent and Trademark Office if filed before the mailing date of a Final Office Action under C.F.R. §1.113, a Notice of Allowance under 37 C.F.R. §1.311, or other Office Actions which close prosecution in the application, provided that the Statement is accompanied by either (1) the statement specified in 37 C.F.R. §1.97(e) or (2) the fee as set forth in C.F.R. §1.17(p). The fee as set forth in C.F.R. §1.17(p) is \$180.00 (ONE-HUNDRED EIGHTY DOLLARS) and a check for this amount is enclosed.

In accordance with their duty of disclosure under 37 C.F.R. § 1.56, applicants would like to direct the Examiner's attention to the documents which are listed on the attached Form PTO-1449 (Exhibit 1) and attached hereto as Exhibits 2-13:

06/06/2003 SZEWDIE1 00000107 09898417

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180.00 OP

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1. Abbot, G.W. et al., "MiPR1 forms  $I_{kr}$  potassium channels with HERG and is associated with cardiac arrhythmia cell," *Cell*, (1999), 97(2):175-187; (**Exhibit 2**)
2. Accili E.A. et al., "Properties and modulation of  $I_f$  in newborn versus adult cardiac SA node," *Am. J. Physiol*, (1991), 272:1549-1552; (**Exhibit 3**)
3. Accili, E.A. et al., "Differential control of the hyperpolarization-activated current ( $I_f$ ) by intracellular cAMP and phosphates inhibition," *J. Physiol*, (1996) 491:115; (**Exhibit 4**)
4. Altomare C, et al., "Integrated allosteric model of voltage gating of HCN channels," *J Gen Physiol*, (2001) 117(6):519-32; (**Exhibit 5**)
5. Altomare C, et al., "Allosteric Voltage-Dependent Gating of HCN Channels," (**abstract**); (**Exhibit 6**)
6. DiFrancesco, D. "Generation and control of cardiac pacing: the pacemaker current," *Trends Cardiovasc. Med*, (1991), 1:250-255; (**Exhibit 7**)
7. Ellingsen, O. et al., "Adult rat ventricular myocytes cultured in defined medium: phenotype and electromechanical function," *Am. J. Physiol*, (1993), 265(2): 747-754; (**Exhibit 8**)
8. Porciatti, F. et al., "The Pacemaker Current  $I_f$  in single

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human atrial myocytes and the effect of beta-adrenoceptor and A1-adenosine receptor simulation," *Br J Pharmacol*, (1991), 122(6): 963-969; (**Exhibit 9**)

9. Shi, W. et al., "The distribution and prevalence of HCN isoforms in the canine heart and their relation to the voltage dependence of  $I_f$ ," (**Abstract**); (**Exhibit 10**)
10. Vassalle, M. et al., Pacemaker channels and cardiac automaticity In "Cardiac Electrophysiology. From Cell to Bedside", Eds. (Zipes D. and Jalife W.B. Saunders Co. Philadelphia, PA, 2000, pages 94-103); (**Exhibit 11**)
11. Wainger, B.J. et al., "Molecular mechanism of cAMP modulation of HCN pacemaker channels," *Nature*, (2001), 411(6839):805-10. (**Exhibit 12**) and
12. Michael R. Rosen, et al., "A High Throughput Biological Heart Rate Monitor That is Molecularly Determined," U.S. Serial No. 09/875,392, filed June 6, 2001. (**Exhibit 13**).

Applicants have submitted only the abstracts for **Exhibits 6** and **10** listed above since the full articles were never published.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

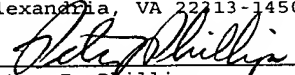
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No fee, other than the enclosed fee of \$180.00 for a Supplemental Information Disclosure Statement, is deemed necessary in connection with the filing of this Second Supplemental Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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